Surprise finding redraws 'map' of blood cell production

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Drs Maria Kauppi (left) and Ashley Ng from the Walter and Eliza Hall Institute in Melbourne, Australia, study blood 'progenitor' cells, which expand and mature in times of stress to replace lost or damaged blood cells. Credit: Walter and Eliza Hall Institute

A study of the cells that respond to crises in the blood system has yielded a few surprises, redrawing the 'map' of how blood cells are made in the body.

The finding, by researchers from the Walter and Eliza Hall Institute, could have wide-ranging implications for understanding blood diseases such as myeloproliferative disorders (that cause excess production of blood cells) as well as used to develop new ways of controlling how blood and clotting cells are produced.

The research team, led by Drs Ashley Ng and Maria Kauppi from the institute's Cancer and Haematology division, investigated subsets of blood 'progenitor' cells and the signals that cause them to expand and develop into mature blood cells. Their results are published today in the journal Proceedings of the National Academy of Sciences of the United States of America.

Dr Ng describes blood progenitor cells as the 'heavy lifters' of the blood system.

"They are the targets for blood cell hormones, called cytokines, which Professor Don Metcalf and colleagues have shown to be critical for regulating blood cell production," Dr Ng said. "In times of stress, such as bleeding, during infection or after chemotherapy, it is really the progenitor cells that respond by replacing lost or damaged blood cells."

Dr Kauppi said the research team was particularly interested in myeloid progenitor cells, which produce megakaryocytes, a type of bone marrow cell that gives rise to blood-clotting platelets. "We used a suite of cell surface markers specific to these progenitor cells that allowed us to isolate and characterise the cells," she said.

The researchers were surprised to find that progenitor cells believed only to be able to produce megakaryocytes were also able to develop into red blood cells.

"We were able to clearly demonstrate that these mouse megakaryocyte progenitor cells have the potential to develop into either megakaryocytes or red blood cells in response to cytokines such as thrombopoietin and erythropoietin, which was quite unexpected," Dr Ng said. "In addition, we discovered that other progenitor populations thought to really only make neutrophils and monocytes [other immune cells], were capable of making red blood cell and platelets really well. In effect, we will have to

redraw the map as to how red cells and platelets are made in the bone marrow."

Dr Kauppi said the researchers found they could regulate whether the progenitor cell became a megakaryocyte or a red blood cell by using different combinations of cytokines. "Now that we have properly identified the major cells and determined how they respond to cytokine signals involved in red blood cell and platelet production, the stage is set for understanding how these progenitors are affected in health and disease," she said. "We can also better understand, for instance, how genetic changes may lead to the development of certain blood diseases."

Dr Ng said the findings would also help researchers discover new ways in which the progenitor cells can be controlled.

"This research is the first step in the future development of treatments for patients with blood diseases," Dr Ng said. "This may occur either by limiting blood cell production when too many are being made, as with myeloproliferative disorders, or stimulating blood production when the blood system is compromised, such as during cancer treatment or infection." Dr Ng said.

Provided by Walter and Eliza Hall Institute